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AMENDMENTS TO THE CLAIMS

Docket No.: 14090-00003-US1

This listing of the claims will replace all prior versions and listings of the claims in this application.

Listing of the Claims:

1. (Currently amended) A compound of the formula (I):

$$R^{2} \xrightarrow{N} X \xrightarrow{4 \text{ 5}} Z \longrightarrow N \xrightarrow{R^{3}} O - R^{4}$$
Formula I

wherein

R¹ is selected from the group consisting of: H, alkyl, alkenyl, alkynyl, haloalkyl, haloalkenyl, heteroalkyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, arylalkyl, heteroarylalkyl, arylalkenyl, cycloalkylalkyl, heterocycloalkylalkyl, heteroaryl, heteroarylheteroalkyl, heterocycloalkylheteroalkyl, cycloalkylheteroalkyl, arylheteroalkyl, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxyaryl, alkenyloxy, alkynyloxy, cycloalkylkoxy, heterocycloalkyloxy, aryloxy, heteroaryloxy, arylalkyloxy, amino, alkylamino, aminoalkyl, acylamino, arylamino, phenoxy, benzyloxy, COOH, alkoxycarbonyl, alkylaminocarbonyl, sulfonyl, alkylsulfonyl, alkylsulfinyl, arylsulfonyl, arylsulfinyl, aminosulfonyl, SR4 and acyl, each of which may be unsubstituted or substituted with one or more substituents independently selected from the group consisting of: halogen, =O, =S, -CN, -NO₂, -CF₃, -OCF₃, alkyl, alkenyl, alkynyl, haloalkyl, haloalkenyl, haloalkynyl, heteroalkyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, hydroxy, hydroxyalkyl, alkoxyalkyl, alkoxyaryl, alkoxyheteroaryl, alkenyloxy, alkynyloxy, cycloalkyloxy, cycloalkenyloxy, heterocycloalkyloxy, heterocycloalkenyloxy, aryloxy, heteroaryloxy, arylalkyl, heteroarylalkyl, arylalkyloxy, -amino, alkylamino, acylamino, aminoalkyl, arylamino, sulfonyl, alkylsulfonyl, arylsulfonyl, arylsulfinyl, aminosulfonyl, aminoalkyl, alkoxyalky, -COOH, -C(O)OR⁵, -COR⁵, -SH, -SR⁶, -OR⁶ and acyl;

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or $R^1 = L$;

R² is selected from the group consisting of: H, halogen, alkyl, alkenyl, alkynyl, haloalkyl, haloalkenyl, heteroalkyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl, heteroaryl, cycloalkylalkyl, cycloalkylheteroalkyl, heterocycloalkylheteroalkyl, heteroarylheteroalkyl, arylheteroalkyl hydroxy, alkynyloxy, cycloalkylkoxy, alkoxyalkyl, alkoxyaryl, alkenyloxy, hydroxyalkyl, alkoxy, heterocycloalkyloxy, aryloxy, heteroaryloxy, arylalkyloxy, amino, alkylamino, aminoalkyl, acylamino, arylamino, phenoxy, benzyloxy, COOH, alkoxycarbonyl, alkylaminocarbonyl, sulfonyl, alkylsulfonyl, alkylsulfinyl, arylsulfonyl, arylsulfinyl, aminosulfonyl, SR⁵ and acyl, each of which may be unsubstituted or substituted with one or more substituents independently selected from the group consisting of: halogen, =O, =S, -CN, -NO₂, -CF₃, -OCF₃, alkyl, alkenyl, alkynyl, haloalkyl, haloalkenyl, haloalkynyl, heteroalkyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxyaryl, alkoxyheteroaryl, alkenyloxy, alkynyloxy, cycloalkyloxy, cycloalkenyloxy, heterocycloalkyloxy, heterocycloalkenyloxy, aryloxy, heteroaryloxy, arylalkyl, heteroarylalkyl, arylalkyloxy, -amino, alkylamino, acylamino, aminoalkyl, arylamino, sulfonyl, alkylsulfonyl, arylsulfonyl, aminosulfonyl, aminoalkyl, alkoxyalky, -COOH, -COR5, -C(O)OR5, -SH, -SR5, -OR6and acyl; or $R^2 = L$;

R³ is selected from the group consisting of H, C₁ -C₆ alkyl, and acyl; or a metal ion selected from sodium, calcium, magnesium;

X and Y are the same or different and are independently selected from the group consisting of: H, halogen, -CN, -NO₂, -CF₃, -OCF₃, alkyl, alkenyl, alkynyl, haloalkyl, haloalkynyl, haloalkynyl, heteroalkyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxyaryl, alkoxyheteroaryl, alkenyloxy, alkynyloxy, cycloalkyloxy, cycloalkenyloxy, heterocycloalkyloxy, heterocycloalkenyloxy, aryloxy, heteroaryloxy, arylalkyl, heteroarylalkyl, arylalkyloxy, -amino, alkylamino, acylamino, aminoalkyl, arylamino, sulfonyl, alkylsulfonyl, arylsulfonyl, aminosulfonyl, aminoalkyl, alkoxyalky, -COOH – C(O)OR⁵, -COR⁵, -SH, -SR⁶, -OR⁶ acyl and -NR⁷R⁸;

Each R⁴ is selected from the group consisting of: H, alkyl, alkenyl, alkynyl, haloalkyl, heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl and acyl;

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Each R⁵ is independently selected from the group consisting of: alkyl, alkenyl, alkynyl, haloalkyl, heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl and acyl;

Each R⁶ is independently selected from the group consisting of: alkyl, alkenyl, alkynyl, haloalkyl, heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl and acyl;

Each R⁷ and R⁸ are each independently selected from the group consisting of: H, alkyl, alkenyl, alkynyl, haloalkyl, heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl and acyl;

L is selected from the group consisting of:

Wherein

Cy is C₁-C₁₅ alkyl, aminoalkyl, heterocycloalkyl, cycloalkyl, aryl, aryloxy or heteroaryl any of which may be optionally substituted one or more substituents independently selected from the group consisting of: halogen, =O, =S, -CN, -NO2, -CF3, -OCF3, alkyl, alkenyl, alkynyl, haloalkyl, haloalkenyl, haloalkynyl, heteroalkyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxyaryl, heteroaryl. hydroxy, alkynyloxy, cycloalkyloxy, cycloalkenyloxy, alkoxyheteroaryl, alkenyloxy, heterocycloalkyloxy, heterocycloalkenyloxy, aryloxy, heteroaryloxy, arylalkyl, heteroarvlalkyl, arylalkyloxy, -amino, alkylamino, acylamino, aminoalkyl, arylamino, sulfonyl, alkylsulfonyl, arylsulfonyl, aminosulfonyl, aminoalkyl, alkoxyalky, -COOH, -C(O)OR⁵, -COR⁵, -SH, -SR⁶, -OR⁶ and acyl.

 L^1 is selected from the group consisting of C_1 – C_5 alkyl, which may be optionally substituted with one or more substituents independently selected from the group consisting of: halogen; =O; =S; -CN; -NO₂; alkyl, alkoxy, acylamino, and alkylamino;

W is selected from the group consisting of a single bond, -O-, -S-, -S(O)-, -S(O)₂-, -N(R⁹)-, -C(O)N(R⁹)-, -SO₂N(R⁹)-, N(R⁹)C(O)-, N(R⁹)SO₂-, and -N(R⁹)-C(O)-N(R¹⁰)-;

b)
$$L=Cy-L^1-W-L^2$$

Wherein,

Cy is C₁-C₁₅ alkyl, aminoalkyl, heterocycloalkyl, cycloalkyl, aryl, aryloxy or heteroaryl any of which may be optionally substituted one or more substituents independently selected from the group consisting of: halogen, =O, =S, -CN, -NO₂, -CF₃, -OCF₃, alkyl, alkenyl, alkynyl, haloalkyl, haloalkenyl, haloalkynyl, heteroalkyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroarvl. hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxyaryl, alkoxvheteroarvl. alkenyloxy, alkynyloxy, cycloalkyloxy, cycloalkenyloxy, heterocycloalkyloxy, heterocycloalkenyloxy, aryloxy, heteroaryloxy, arylalkyl, heteroarylalkyl, arylalkyloxy, -amino, alkylamino, acylamino, aminoalkyl, arylamino, sulfonyl, alkylsulfonyl, arylsulfonyl, aminosulfonyl, aminoalkyl, alkoxvalky, -COOH, C(O)OR5, -COR5, -SH, -SR5, -OR6and acyl;

 L^1 and L^2 are the same or different and independently C_1 – C_5 alkyl, which may be optionally substituted with one or more substituents independently selected from the group consisting of: halogen; =O; =S; -CN; -NO₂; -CF₃, -OCF₃, alkyl, alkoxy, acylamino and alkylamino;

W is selected from the group consisting of a single bond, -O-, -S-, -S(O)-, -S(O)₂-, -N(R⁹)-, -C(O)N(R⁹)-, -SO₂N(R⁹)-, N(R⁹)C(O)-, N(R⁹)SO₂-, and -N(R⁹)-C(O)-N(R¹⁰)-;

c) $L=Cy-(CH_2)m-W-$ Wherein,

Cy is C₁-C₁₅ alkyl, aminoalkyl, heterocycloalkyl, cycloalkyl, aryl, aryloxy or heteroaryl any of which may be optionally substituted one or more substituents independently selected from the group consisting of: : halogen, =O, =S, -CN, -NO2, -CF3, -OCF3, alkyl, alkenyl, alkynyl, haloalkyl, haloalkenyl, haloalkynyl, heteroalkyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxyaryl, heteroaryl, hydroxy, cycloalkyloxy, cycloalkenyloxy, alkoxyheteroaryi, alkenyloxy, alkynyloxy, heterocycloalkyloxy, heterocycloalkenyloxy, aryloxy, heteroaryloxy, arylalkyl, heteroarvlalkyl, arylalkyloxy, -amino, alkylamino, acylamino, aminoalkyl, arylamino, sulfonyl, alkylsulfonyl, arylsulfonyl, aminosulfonyl, aminoalkyl, alkoxyalky, -COOH, C(O)OR5, -COR5, -SH, -SR5, -OR6and acyl;

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m is 0, 1, 2, 3, 4 or 5;

W is selected from the group consisting of a single bond, -O-, -S-, -S(O)-, $-S(O)_{2}$, $-N(R^{9})$, $-C(O)N(R^{9})$, $-SO_{2}N(R^{9})$, $N(R^{9})C(O)$, $N(R^{9})SO_{2}$, and $-N(R^{9})$ -C(O)-N(R¹⁰)-;

$L=L^1-W-L^2$ d)

L¹ and L² are the same or different and independently selected from C₁-C₅ alkyl, which may be optionally substituted one or more substituents independently selected from the group consisting of: halogen; =O; =S; -CN; -NO₂; -CF₃, -OCF₃, alkyl, alkoxy, acylamino, alkylamino;

W is selected from the group consisting of a single bond, -O-, -S-, -S(O)-, $-S(O)_{2^{-}}$, $-N(R^{9})_{-}$, $-C(O)N(R^{9})_{-}$, $-SO_{2}N(R^{9})_{-}$, $N(R^{9})C(O)_{-}$, $N(R^{9})SO_{2^{-}}$, and $-N(R^{9})_{-}$ C(O)-N(R¹⁰)-;

R⁹ and R¹⁰ are the same or different and are independently selected from H, C₁-C₆ alkyl, C₄-C₉ cycloalkyl, C₄-C₉ heterocycloalkyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl; and acyl;

Z is selected from -CH₂-, -CH₂CH₂-, -CH=CH-, or C₃-C₆ cycloalkyl, unsubstituted or substituted with one or more substituents independently selected from the group consisting of C₁-C₄ alkyl;

or a pharmaceutically acceptable salt thereof.

- (Currently amended) A compound of according to claim 1 wherein Z is a bond, -CH2-, 2. -CH₂CH₂-, or -CH=CH-, or C₃-C₆ cycloalkyl, and Z is attached at ring position 5 or 6.
- (Currently amended) A compound of according to claim 1 or 2 wherein Z is -CH=CH-, 3. and is attached at ring position 5.
- (Currently amended) A compound of any one of claims 1 to 3 according to claim 1 4. wherein $R^3 = H$.
- (Currently amended) A compound of any one of claims 1 to 4 according to claim 1 5. wherein X and Y = H.

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6. (Currently amended) A compound according to any one of claims 1 to 5 claim 1 wherein $R^4 = H$.

- 7. (Currently amended) The compound according to any one of claims 1 to 6 claim 1 wherein R¹ is selected from the group consisting of: H, hydroxyalkyl, alkyl, arylalkyl, heteroarylalkyl, alkoxyalkyl, aminoalkyl, and heterocycloalkyl, each of which may be unsubstituted or substituted.
- 8. (Currently amended) The compound according to any one of claims 1 to 7 claim 1 wherein R¹ is selected from the group consisting of: H; methyl; (pyridin-2-yl)methyl; (pyridin-3-yl)methyl; ethyl; 2-hydroxy-ethyl; 2-(pyridin-2-yl)ethyl; 2-(pyridin-3-yl)ethyl; 2-phenyl-ethyl; 2-carboxy-ethyl; 2-(morpholin-4-yl)-ethyl; 2-(piperidin-1-yl)-ethyl; 2-(pyrollidin-1-yl)-ethyl; 2-diethylamino-ethyl; propyl; 2,3-di-hydroxy-propyl; 3-hydroxy-propyl; 3-methoxy-propyl; 3-isopropoxy-propyl; 2,2-dimethyl-propyl; 3-dimethylamino-propyl; 3-dimethylamino-2,2-dimethyl-propyl; 3-(2-oxo-pyrollidin-1-yl)-propyl; 3-(morpholin-4-yl)-propyl; 3-(imadazol-1-yl)-propyl; 3-(4-methyl-piperidin-1-yl)-propyl; 3-(pyrollidin-1-yl)-propyl; 4-dimethylamino-butyl; 5-hydroxy-pentyl; allyl; benzyl; 3,4,5-trimethoxybenzyl.
- 9. (Currently amended) A compound according to any one of claims 1 to 8 claim 1 wherein R² is selected from the group consisting of H, alkyl, arylalkyl, aryl, heteroaryl, heteroalkyl, cycloalkyl, each of which may be unsubstituted or substituted.
- 10. (Currently amended) A compound according to any-one-of-claims 1 to 9 claim 1 wherein R² is,: H; methyl; benzylamino-methyl; dibenzylamino-methyl; [2-(4-fluoro-phenyl)-acetylamino]-methyl; [2-(4-methoxy-phenyl)-acetylamino]-methyl; 4-methoxy-benzylamino-methyl; benzyloxy-methyl; phenylacetylamino-methyl; 1-amino-2-phenyl-ethyl; 2-benzylamino-ethyl; 2-(3-methoxy-phenyl)-ethyl; 2-(pyridin-3-yl)ethyl; 2-(2-phenoxyacetylamino)-ethyl; 2-benzenesulphonylamino-ethyl; 2-phenyl-ethyl; isopropyl; 2-phenyl-propyl; 3-phenyl-propyl; 3-phenoxy-propyl; 3-(1H-indol-3-yl)-propyl; 4-methoxy-phenyl; 4-fluoro-phenyl; 4-benzyloxy-3-methoxy-phenyl; isobutyl; cyclohexyl; octyl; benzyl; pyridin-2-yl; pyridin-4-yl; thiophen-3-yl; benzylsulfanyl, and 2-phenylmethansulfanyl.

11. (Currently amended) The compound of claim 1 wherein the compound is selected from compounds, and their pharmaceutically acceptable salts, selected from the group consisting of

N-Hydroxy-3-[1-(3-hydroxy-propyl)-2-(2-phenyl-propyl)-1*H*-benzimidazol-5-yl]-acrylamide

N-Hydroxy-3-[1-(3,4,5-trimethoxybenzyl)-2-(2-phenyl-ethyl)-1*H*-benzimidazol-5-yl]-acrylamide

N-Hydroxy-3-[2-(4-benzyloxy-3-methoxy-phenyl)-1-methyl-1*H*-benzimidazole-5-yl]-acrylamide

N-Hydroxy-3-[2-(4-benzyloxy-3-methoxy-phenyl)-1-(3-hydroxy-propyl)-1*H*-benzimidazole-5-yl]-acrylamide

N-Hydroxy-3-[1-(2-hydroxy-ethyl)-2-(4-methoxy-phenyl)-1*H*-benzimidazole-5-yl]-acrylamide

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N-Hydroxy-3-[1-(2,3-hydroxy-propyl)-2-(4-methoxy-phenyl)-1*H*-benzimidazole-5-yl]-acrylamide

N-Hydroxy-3-[2-(4-benzyloxy-3-methoxy-phenyl)-1-(2,3-hydroxy-propyl)-1*H*-benzimidazole-5-yl]-acrylamide

N-Hydroxy-3-[1-(2,3-hydroxy-propyl)-2-(2-phenylethyl)-1*H*-benzimidazol-5-yl]-acrylamide

N-Hydroxy-3-[1-(2,3-hydroxy-propyl)-2-(2-pyridyl)-1*H*-benzimidazol-5-yl]-acrylamide

N-Hydroxy-3-[1-(2-hydroxy-ethyl)-2-(4-pyridyl)-1*H*-benzimidazol-5-yl]-acrylamide

N-Hydroxy-3-[1-(3-hydroxy-propyl)-2-(4-pyridyl)-1*H*-benzimidazol-5-yl]-acrylamide

N-Hydroxy-3-[1-(3-pyridylmethyl)-2-(2-phenylethyl)-1*H*-benzimidazol-5-yl]-acrylamide

N-Hydroxy-3-[1-(3-hydroxy-propyl)-2-(2-pyridyl)-1*H*-benzimidazol-5-yl]-acrylamide

N-Hydroxy-3-[1-(3-hydroxy-propyl)-2-phenethyl-1*H*-benzimidazol-5-yl]-acrylamide

N-Hydroxy-3-[1-(3-methoxy-propyl)-2-phenethyl-1*H*-benzimidazol-5-yl]-acrylamide Application No.: TBA (Based on PCT/SG2004/000307)

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N-Hydroxy-3-(2-phenethyl-1-(pyridin-2-yl)methyl-1*H*-benzimidazol-5-yl)-acrylamide

N-Hydroxy-3-[1-(3-Dimethylamino-2,2-dimethyl-proppyl)-2-phenethyl-1*H*-benzimidazol-5-yl]-acrylamide

N-Hydroxy-3-[2-phenethyl-1-(2-pyridin-2-yl-ethyl-1*H*-benzimidazol-5-yl]-acrylamide

N-Hydroxy-3-[2-Benzyloxymethyl-1-(3-hydroxy-propyl-1*H*-benzimidazl-5yl]-acrylamide

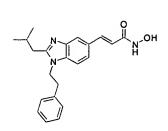
N-Hydroxy-3-[1-(3-hydroxy-propyl)-2-thiophen-3-yl-1*H*-benzimidazol-5-yl]-acrylamide

N-Hydroxy-3-[1-(3-hydroxy-propyl)-2-isobutyl-1*H*-benzimidazol-5-yl]-acrylamide

N-Hydroxy-3-[2-isobutyl-1-(2-pyridin-2-yl-ethyl)-1*H*-benzimidazol-5-yl]-acrylamide

N-Hydroxy-3-[1-(3-hydroxy-propyl)-2-octyl-1*H*-benzimidazol-5-yl]-acrylamide

N-Hydroxy-[2-cyclohexyl-1-(3-hydroxy-propyl)-1*H*-benzimidazol-5-yl]-acrylamide



N-Hydroxy-3-(2-isobutyl-1-phenethyl-1*H*-benzimidazol-5-yl]-acrylamide

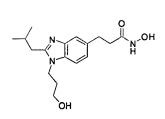
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N-Hydroxy-3-(1,2-Diphenethyl-1*H*-benzimidazol-5-yl]-acrylamide

N-Hydroxy-3-(2-phenethyl-1-(2-pyridin-3-yl-ethyl)-1*H*-benzimidazol-5-yl]-acrylamide

N-Hydroxy-3-[2-Benzyloxymethyl-1-(2-pyridin-3-ethyl)-1*H*-benzimidazol-5-yl]-acrylamide

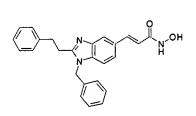


N-Hydroxy-3-[1-(3-Hydroxy-propyl)-2-isobutyl-1*H*-benzimidazol-5-yl]-propionamide

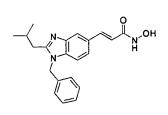
N-Hydroxy-3-{1-[3-(2-oxo-pyrrolidin-1-yl)-propyl]-2-phenethyl-1*H*-benzimidazol-5-yl}-acrylamide

N-Hydroxy-3-[1-(3-morpholin-4-propyl]-2-phenethyl-1*H*-benzimidazol-5-yl}-acrylamide

3-[5-(2-Hydrocarbamoyl-vinyl)-2-phenethyl-1*H*-benzimidazol-1-yl]-propionic acid



N-Hydroxy-3-(1-Benzyl-2-phenethyl-1*H*-benzimidazol-5-yl}-acrylamide



N-Hydroxy-3-(1-Benzyl-2-isobutyl-1*H*-benzimidazol-5-yl}-acrylamide

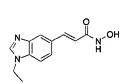
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N-Hydroxy-3-(1-benzyl-1*H*-benzimidazol-5-yl}-acrylamide

N-Hydroxy-3-(2-phenethyl-1-propyl-1*H*-benzimidazol-5-yl}-acrylamide

N-Hydroxy-3-(1-propyl-1H-benzimidazol-5-yl}-acrylamide

N-Hydroxy-3-(1-Ethyl-2-phenethyl-1*H*-benzimidazol-5-yl}-acrylamide

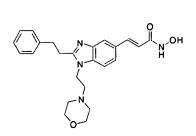


N-Hydroxy-3-(1-Ethyl-1*H*-benzimidazol-5-yl}-acrylamide

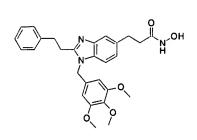
N-Hydroxy-3-[2-(2-phenyl-propyl)-1-(2-pyridin-3-yl-ethyl)-1*H*-benzimidazol-5-yl]-acrylamide

N-Hydroxy-3-[1-(2-pyridin-2-yl-ethyl)-1*H*-benzimidazol-5-yl]-acrylamide

N-Hydroxy-3-(1-Ethyl-2-methyl-1*H*-benzimidazol-5-yl]-acrylamide



N-Hydroxy-3-[1-(2-morpholin-4-yl-ethyl)-2-phenethyl-1*H*-benzimidazol-5-yl]-acrylamide

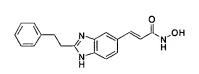


N-Hydroxy-3-[2-phenethyl-1-(3,4,5-trimethoxybenzyl)-1*H*-benzimidazol-5-yl]-propionamide

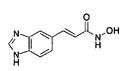
N-hydroxy-3-[1-(3-hydroxy-propyl)-2-isopropyl-1*H*-be<u>n</u>zimidazol-5-yl]-acrylamide

N-Hydroxy-3-(1-methyl-2-phenethyl-1*H*-benzimidazol-5-yl)-acrylamide

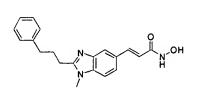
N-Hydroxy-3-(1-methyl-1*H*-benzimidazol-5-yl)-acrylamide



N-Hydroxy-3-(2-phenethyl-1*H*-benzimidazol-5-yl)-acrylamide



N-Hydroxy-3-(1H-benzimidazol-5-yl)-acrylamide



N-Hydroxy-3-[1-methyl-2-(3-phenyl-propyl)-1*H*-benzimidazol-5-yl]-acrylamide

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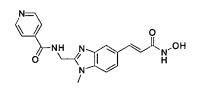
N-Hydroxy-3-(1,2-dimethyl-1H-benzimidazol-5-yl]-

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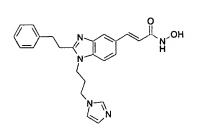
N-Hydroxy-3-[1-methyl-2-(phenylacetylaminomethyl)-1*H*-benzimidazol-5-yl]-acrylamide

acrylamide

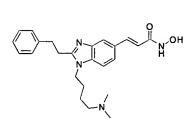
N-[5-(2-Hydroxycarbomoyl-vinyl)-1-methyl-1*H*-benzimidazol-2-ylmethyl]-isonicotinamide



N-Hydroxy-3-[1-(3-imidazol-1-yl-propyl)-2-phenethyl-1*H*-benzimidazol-5-yl]-acrylamide

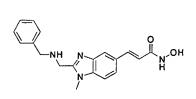


N-Hydroxy-3-[1-(4-dimethylamino-butyl)-2-phenethyl-1*H*-benzimidazol-5-yl]-acrylamide

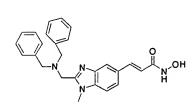


N-Hydroxy-3-(3-benzyl)-2-phenethyl-3*H*-benzimidazol-5-yl]-acrylamide

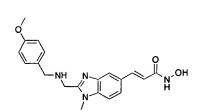
N-Hydroxy-3-(3-methyl-2-phenethyl-3*H*-benzimidazol-5-yl]-acrylamide



N-Hydroxy-3-[2-(benzylamino-methyl)-1-methyl-1*H*-benzimidazol-5-yl]-acrylamide



N-Hydroxy-3-{2-[(dibenzylamino)-methyl]-1-methyl-1*H*-benzimidazol-5-yl}-acrylamide

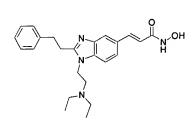


N-Hydroxy-3-{2-[(4-methoxy-benzylamino)-methyl]-1-methyl-1*H*-benzimidazol-5-yl}-acrylamide

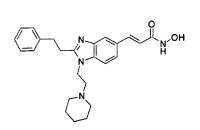
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N-Hydroxy-3-[2-(benzylamino-methyl)-ethyl-1*H*-benzimidazol-5-yl]-acrylamide

N-Hydroxy-3-(2-(benzyl-1-methyl-3-oxo-1*H*-benzimidazol-5-yl)-acrylamide



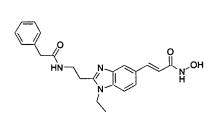
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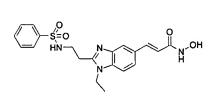
N-Hydroxy-3-[2-phenethyl-1-(piperidin-1-yl-ethyl)-1*H*-benzimidazol-5-yl]-acrylamide

N-Hydroxy-3-{2-[(dibenzylamino)-methyl]-1-ethyl-1*H*-benzimidazol-5-yl}-acrylamide

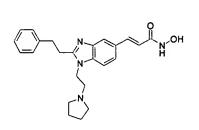
N-Hydroxy-3-(2-{[2-(4-fluoro-phenyl)-acetylamino]-methyl}-1-methyl-1*H*-benzimidazol-5-yl)-acrylamide



N-Hydroxy-3-[1-ethyl-2-(2-phenylacetylamino-ethyl)-1*H*-benzimidazol-5-yl]-acrylamide



N-Hydroxy-3-[2-(2-Benzenesulfonylamino-ethyl)-1-ethyl-1*H*-benzimidazol-5-yl]-acrylamide



N-Hydroxy-3-[2-phenyethyl-1-(2-pyrrolidin-1-ylethyl)-1*H*-benzimidazol-5-yl]-acrylamide

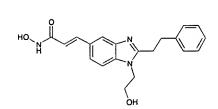
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N-Hydroxy-3-{1-ethyl-2-[2-(2-phenoxy-acetylamino)-ethyl]-1*H*-benzimidazol-5-yl]-acrylamide

N-Hydroxy-3-[2-(2-benzylamino-ethyl)-1-ethyl--1*H*-benzimidazol-5-yl]-acrylamide

N-Hydroxy-3-[1-(2,2-dimethyl-propyl)-2-phenethyl-1*H*-benzimidazol-5-yl]-acrylamide

N-Hydroxy-3-[1-(1-Benzyl-piperidin-4-yl)-2-phenethyl-1*H*-benzimiazo-5-yl]acrylamide

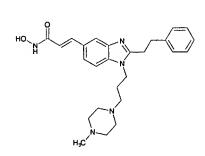


N-Hydroxy-3-[1-(2-hydroxyethyl)-2-phenethyl-1*H*-benzimidazol-5-yl]-acrylamide

N-Hydroxy-3-[1-(5-hydroxy-pentyl)-2-phenthyl-1*H*-benzimidazol-5-yl]-acrylamide

N-Hydroxy-3-(1-allyl-2-phenethyl-1*H*-benzimidazol-5-yl)-acrylamide

N-Hydroxy-3-(1-(3-isoproxy-propyl)-2-phenethyl-1*H*-benzimidazol-5-yl)-acrylamide



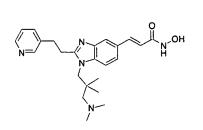
N-Hydroxy-3-{1-[3-(4-methyl-piperzin-1-yl)-2-phenethyl-1*H*-benzimidazol-5-yl}-acrylamide

N-Hydroxy-3-[2-phenethyl-1-(3-pyrrolidin-1-yl-propyl)-1*H*-benzimidazol-5-yl]-acrylamide

N-Hydroxy-3-[1-(3-Dimethylamino-2,2-dimethyl-propyl)-2-(3-phenyl-propyl)-1*H*-benzimidazol-5-yl]-acrylamide

N-Hydroxy-3-{1-(3-Dimethylamino-2,2-dimethyl-propyl)-2-[2-(4-fluoro-phenyl)-ethyl]-1*H*-benzimidazol-5-yl]-acrylamide

N-Hydroxy-3-{2-(4-fluoro-phenyl)-ethyl]-1*H*-benzimidazol-5-yl}-acrylamide



N-Hydroxy-3-[1-(3-Dimethylamino-2,2-dimethyl-propyl)-2-(2-pyridin-3-yl-ethyl)-1*H*-benzimidazol-5-yl]-acrylamide

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N-Hydroxy-3-[2-(2-pyridin-3-yl-propyl)-1*H*-benzimidazol-5-yl]-acrylamide

2-[2-Phenethyl-1-(3,4,5-trimethoxy-benzyl)-1*H*-benzimidazol-5-yl]-cyclopropanecarboxylic acid hydroxyamide

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N-Hydroxy-3-[2-benzylsulfanyl-1-(3-dimethylamino-2-2,dimethyl-propyl)-1*H*-benzimidazol-5-yl]-acrylamide

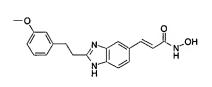
N-Hydroxy-3-[1-(2-piperidin-1-yl-ethyl)-1*H*-benzimidazol-5-yl]-acrylamide

N-Hydroxy-3-[1-(3-dimethylamino-2,2-dimethyl-propyl)-2-phenylmethanesulfonyl-1*H*-benzimidazol-5-yl]-acrylamide

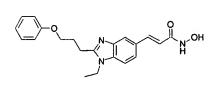
N-Hydroxy-3-(2-benzyl-1-ethyl-1*H*-benzimidazol-5-yl)-acrylamide

N-Hydroxy-3-{1-ethyl-2-[3-(1H-indol-3-yl)-propyl]-1*H*-benzimidazol-5-yl)-acrylamide

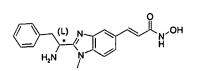
N-Hydroxy-3-{1-(3-dimethylamino-2,2-dimethyl-propyl)-2-[2-(3-methoxy-phenyl)-ethyl]-1*H*-benzimidazol-5-yl)-acrylamide



N-Hydroxy-3-{2-(3-methoxy-phenyl)-ethyl]-1*H*-benzimidazol-5-yl}-acrylamide



N-Hydroxy-3-[1-ethyl-2-(3-phenoxy-propyl)-1*H*-benzimidazol-5-yl]-acrylamide



(*L*)-*N*-Hydroxy-3-[2-(1-amino-2-phenyl-ethyl)-1-methyl-1*H*-benzimidazol-5-yl]-acrylamide

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N-Hydroxy-3-(2-{[2-(4-methoxy-phenyl)-acetylamino]-methyl}-1-methyl-1*H*-benzimidazol-5-yl)-acrylamide

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2-(1-Methyl-2-phenethyl-1*H*-benzimidazol-5-yl)-cyclopropanecarboxylic acid hydroxyamide

- 12. (Currently amended) A pharmaceutical composition including a compound according to any one of claims 1 to 11 claim 1 and a pharmaceutically acceptable diluent, excipient or carrier.
- 13. (Currently amended) A method of Use of a compound according to any one of claims 1 to 11 in the preparation of a medicament for the treatment of a disorder caused by, associated with or accompanied by disruptions of cell proliferation and/or angiogenesis in a patient the method including administration of a therapeutically effective amount of a compound according to claim 1 to the patient.
- 14. (Currently amended) A <u>method</u> use according to claim 13 wherein the disorder is a proliferative disorder.
- 15. (Currently amended) A <u>method</u> use according to claim 14 13 wherein the proliferative disorder is cancer.
- 16. (Currently amended) A-method of treatment of a disorder caused by, associated with or accompanied by disruptions of cell proliferation and/or angiogenesis in a patient the method including administration of a therapeutically effective amount of a compound according to any one of claims 1 to 11 to the patient Use of a compound according to claim 1 or a pharmaceutical composition according to claim 12 to modify deacetylase activity.

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17. (Currently amended) A <u>use method</u> according to claim 16 wherein the <u>deacetylase</u> activity is histone deacetylace activity disorder is a proliferative disorder.

- 18. (Currently amended) A <u>use method</u> according to claim 16 wherein the <u>deacetylase</u> activity is class I histone deacetylase <u>activity disorder is cancer</u>.
- 19. (Currently amended) A use Use of a compound according to any one of claims 1 to 11 claim 17 wherein the histone deacetylase is HDAC1 or a pharmaceutical composition according to claim 12 to modify deacetylase activity.
- 20. (Currently amended) A use according to claim 19 17 wherein the deacetylase activity is histone deacetylase is HDAC8 activity.
- 21. (Currently amended) A use according to claim 19 wherein the deacetylase activity is class I histone deacetylase activity method of treatment of a disorder that can be treated by the inhibition of histone deacetylase in a patient including administration of a therapeutically effective amount of a compound according to claim 1 to the patient.
- 22. (Currently amended) A method use according to claim 20 or 21 wherein the histone deacetylase is HDAC1 disorder is selected from the group consisting of proliferative disorders (e.g. cancer); Neurodegenerative diseases including Huntington's Disease, Polyglutamine disease, Parkinson's Disease, Alzheimer's Disease, Seizures, Striatonigral degeneration, Progressive supranuclear palsy, Torsion dystonia, Spasmodic torticollis and dyskinesis, Familial tremor, Gilles de la Tourette syndrome, Diffuse Lewy body disease, Progressive supranuclear palsy, Pick's disease, Intracerebral haemorrhage, Primary lateral sclerosis, Spinal muscular atrophy, Amyotrophic lateral sclerosis, Hypertrophic interstitial polyneuropathy, Retinitis pigmentosa, Hereditary optic atrophy, Hereditary spastic paraplegia, Progressive ataxia and Shy-Drager syndrome; Metabolic diseases including Type 2 diabetes; Degenerative Diseases of the Eye including Glaucoma, Age-related macular degeneration, Rubeotic glaucoma; Inflammatory diseases and/or Immune system disorders including Rheumatoid Arthritis (RA). Osteoarthritis, Juvenile chronic arthritis, Graft versus Host disease, Psoriasis, Asthma,

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Spondyloarthropathy, psoriasis, Crohn's Disease, Inflammatory bowel disease, Colitis Ulcerosa, Alcoholic hepatitis, Diabetes, Sjoegrens's syndrome, Multiple Sclerosis, Ankylosing spondylitis, Membranous glomerulopathy, Discogenic pain, Systemic Lupus Erythematosus; Disease involving angiogenesis including cancer, psoriasis, rheumatoid arthritis; Psychological disorders including bipolar disease, schizophrenia, mania, depression and dementia; Cardiovascular Diseases including Heart failure, restenosis and arteriosclerosis; Fibrotic diseases including liver fibrosis, cystic fibrosis and angiofibroma; Infectious diseases including Fungal infections, such as Candida Albicans, Bacterial infections, Viral infections, such as Herpes Simplex, Protozoal infections, such as Malaria,-Leishmania infection, Trypanosoma brucei infection, Toxoplasmosis and coccidiosis and Haematopoietic disorders including thalassemia, anemia and sickle cell anemia.

- 23. (Currently amended) A use according to claim 20 or 21 wherein the histone deacetylase is HDAC8 method for inhibiting cell proliferation including administration of an effective amount of a compound according to claim 1.
- 24. (Currently amended) A method of treatment of a <u>neurodegenerative</u> disorder that can be treated by the inhibition of histone deacetylase in a patient including administration of a therapeutically effective amount of a compound according to any one of claims 1 to 11 claim 1 to the patient.
- 25. (Currently amended) A method according to claim 24 wherein the <u>neurodegenerative</u> disorder is selected from the group consisting of Anti-proliferative disorders (e.g. cancer); Neurodegenerative diseases including—Huntington's Disease, Polyglutamine disease, Parkinson's Disease, Alzheimer's Disease, Seizures, Striatonigral degeneration, Progressive supranuclear palsy, Torsion dystonia, Spasmodic torticollis and dyskinesis, Familial tremor, Gilles de la Tourette syndrome, Diffuse Lewy body disease, Progressive supranuclear palsy, Pick's disease, Intracerebral haemorrhage, Primary lateral sclerosis, Spinal muscular atrophy, Amyotrophic lateral sclerosis, Hypertrophic interstitial polyneuropathy, Retinitis pigmentosa, Hereditary optic atrophy, Hereditary spastic paraplegia, Progressive ataxia and Shy-Drager syndrome; Metabolic diseases including Type 2 diabetes; Degenerative Diseases of the Eye including Glaucoma, Age-related macular degeneration, Rubectic glaucoma; Inflammatory

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diseases and/or Immune system disorders including Rheumatoid Arthritis (RA), Osteoarthritis, Juvenile chronic arthritis, Graft versus Host disease, Psoriasis, Asthma, Spondyloarthropathy, psoriasis, Crohn's Disease, Inflammatory bowel disease, Colitis Ulcerosa, Alcoholic hepatitis, Diabetes, Sjoegrens's syndrome, Multiple Sclerosis, Ankylosing spondylitis, Membraneus glomerulopathy, Discogenic pain, Systemic Lupus Erythematosus; Disease involving angiogenesis including cancer, psoriasis, rheumatoid arthritis; Psychological disorders including bipolar disease, schizophrenia, mania, depression and dementia; Cardiovascular Diseases including Heart failure, restenosis and arteriosclerosis; Fibrotic diseases including liver fibrosis, cystic fibrosis and angiofibroma; Infectious diseases including Fungal infections, such as Candida Albicans, Bacterial infections, Viral infections, such as Herpes Simplex, Protozoal infections, such as Malaria, Leishmania infection, Trypanosoma brucei infection, Toxoplasmosis and coccidiosis and Haematopoietic disorders including thalassemia, anemia and sickle cell anemia.

26. (Currently amended) A method <u>of treatment of an inflammatory disease and/or immune system disorder in a patient</u> <u>for inhibiting cell proliferation</u> including administration of <u>a therapeutically an effective amount of a compound according to any one of claims 1 to 11 <u>claim</u> 1 to the patient.</u>

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27. (Currently amended) A method <u>according to claim 26 wherein the inflammatory disease</u> <u>and/or immune system disorder is rheumatoid arthritis</u> of treatment of a neurodegenerative disorder in a patient including administration of a therapeutically effective amount of a compound according to any one of claims 1 to 11 to the patient.

- 28. (Currently amended) A method according to claim 27 26 wherein the <u>inflammatory</u> disease and/or immune system disorder is systemic lupus erythematosus neurodegenerative disorder is Huntington's Disease.
- 29. (Currently amended) A method for measuring an acetylated histone concentration in a biological sample using an enzyme-linked immunosorbant assay, the enzyme-linked immunosorbant assay including a combination of a primary capture antibody, or a portion thereof, and secondary detection antibody, or a portion thereof of treatment of an inflammatory disease and/or immune system disorder in a patient including administration of a therapeutically effective amount of a compound according to any one of claims 1 to 11 to the patient.
- 30. (Currently amended) A method according to claim 29, wherein the <u>primary capture</u> antibody is selected from the group consisting of: an anti-H3 monoclonal antibody, an anti-acetylated H3 polyclonal antibody, a goat anti-H3 polyclonal antibody, a goat anti-acetylated H3 polyclonal antibody and a combination thereof inflammatory disease and/or immune system disorder is rheumatoid arthritis.
- 31. (Currently amended) A method according to claim 29, wherein the <u>secondary detection</u> antibody is <u>selected from the group consisting of: an anti-H3 monoclonal antibody, an anti-acetylated H3 polyclonal antibody, a goat anti-H3 polyclonal antibody, a goat anti-acetylated H3 polyclonal antibody and a combination thereof inflammatory disease and/or immune system disorder is systemic lupus erythematosus.</u>
- 32. (Currently amended) A method <u>according to claim 29, wherein the primary capture antibody is a mouse anti-H3 monoclonal antibody and the secondary detection antibody is a rat anti-acetylated H3 polyclonal antibody for measuring an acetylated histone concentration in a biological sample using an enzyme-linked immunosorbant assay, the enzyme-linked</u>

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immunosorbant assay including a combination of a primary capture antibody, or a portion thereof, and secondary detection antibody, or a portion thereof.

33. (Currently amended) A method according to claim 32, wherein the primary capture antibody is selected from the group consisting of: an anti-H3 monoclonal antibody, an anti-acetylated H3 polyclonal antibody, a goat anti-H3 polyclonal antibody, a goat anti-acetylated H3 polyclonal antibody and a combination thereof for identifying the pharmacological effect of a histone deacetylase inhibitor in a cell, the method including the steps of:

- a) providing a cell that has been treated with a histone deacetylase inhibitor;
- b) measuring the acetylated histone concentration in the cell by a method according to claim 29; and
- c) comparing the acetylated histone concentration with the acetylated histone concentration of a control sample.
- 34. (Currently amended) A method according to claim 32 or 33, wherein the <u>control sample</u> is derived from a cell that has not been treated with a histone deacetylase inhibitor secondary detection antibody is selected from the group consisting of: an anti-H3 monoclonal antibody, an anti-acetylated H3 polyclonal antibody, a goat anti-H3 polyclonal antibody, a goat anti-acetylated H3 polyclonal antibody and a combination thereof.
- 35. (Currently amended) A method according to claim 32 33, wherein the <u>cell is a tumour</u> <u>cell</u> primary capture antibody is a mouse anti-H3 monoclonal antibody and the secondary detection antibody is a rat anti-acetylated H3 polyclonal antibody.
- 36. (Currently amended) A method for identifying the pharmacological effect of a histone deacetylase inhibitor in a <u>subject</u> cell, the method including the steps of:
- a) obtaining a biological sample from a subject providing a cell that has been treated with a histone deacetylase inhibitor;
- b) measuring the acetylated histone concentration in the <u>biological sample</u> cell by a method according to any one of claims <u>claim</u> 32 to 35; and

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c) comparing the acetylated histone concentration with the acetylated histone

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concentration of a control sample.

37. (Currently amended) A method according to claim 36, wherein the control sample is a

biological sample derived from a subject cell that has not been treated with a histone

deacetylase inhibitor.

38. (Currently amended) A method according to claims 36 or 37 claim 32, wherein the

biological sample is selected from the group consisting of tissue, blood, serum, plasma, urine,

saliva and a combination thereof cell is a tumour cell.

39. (Currently amended) A method according to claim 36, wherein the biological sample is

selected from the group consisting of tissue, blood, serum, plasma, urine, saliva and a

combination thereof for identifying the pharmacological effect of a histone-deacetylase inhibitor

in a subject, the method including the steps of:

a) obtaining a biological sample from a subject that has been treated with a histone

deacetylase inhibitor;

b) measuring the acetylated histone concentration in the biological sample by a method

according to any one of claims 32 to 35; and

_____c) comparing the acetylated histone concentration with the acetylated histone

concentration of a control-sample.

40. (Currently amended) A method according to claim 39 36, wherein the control sample is

a biological sample derived from a subject that has not been treated with a histone deacetylase

inhibitor includes a compound according to claim 1.

41. (Canceled)

42. (Canceled)

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